(Transcription of an Edison Voicewriter record from Dr. Lederberg)

Joshua Lederberg
Madison, Wisconsin
April 20, 1957

Dr. Joseph Lein
Bristol Laboratories Inc.
Syracuse, New York

Dear Joe:

It has been some long time since we had any intimate chats with one another and I am just hoping that things are going very well, if very busily.

I am anxious to hear how your preliminary consideration of "substitutional chemotherapy" has been coming along. I still find no good reason to retreat from my zeal for this approach. This recognizes, however, the necessity of continuing to exploit the more traditional methods.

One reason that I was reminded to communicate with you again was a paper in last week's SCIENCE which referred to the occurrence of an antibacterial agent in solutions of tryptophan that had been subject to irradiation. I have no idea whether this itself is going to lead them anywhere, but I was interested that they had in fact embarked on this approach with the hope of finding an anti-metabolite.

The area that may prove the most interesting here, although the technical approach is the most difficult, would be, I think, in the treatment if possible of DNA and the trial of such material in tumor therapy. A lot of work is of course going on on trials with carefully synthesized analogs of nucleic acid components, and some of this may in due course pay off even more than it has until now. However, I think that there is still more room for the more comprehensive, if sloppier, approach that I had been outlining. Would I be asking too much to request some sort of digest of your current thinking about this problem and the specific ways in which you might be considering going about it. I realize that it might be much more fruitful if I could manage a personal contact but, if anything, affairs have been more hectic than ever. We have shifted our plans for Australia somewhat. Our present itinerary will bring us to leave the States on August 1st and we will get back sometime before the end of November. There is a good deal of work going on down there in therapeutic screening, especially for tuberculosis, and you may find something interesting in what I can dig out there.

Our work on L forms, i.e., the growth of protoplasts in agar, is coming to an interesting conclusion. Recently a number of wall-deficient mutants which have arisen in the course of growth of <u>E.coli</u> in the presence of penicillin have been isolated and some of them at least are blocked in the synthesis of diamino pimelic acid. We are looking at others to see if we can pick up other specific wall precursors, the most interesting of which might be a substance carboxyethylglucosamine, which has now been christened Muriamic Acid. We never have received from you a sample of the sulfonic analog of DAP that you had been playing with. Is there any more to say about the possible activity of these compounds?

Yours sincerely,

Joshua Lederberg

JL:jlg